RESEARCH PAPER

Phenelzine Reduces Plasma Vitamin B_6

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Plasma levels of the active form of vitamin B_6 (pyridoxal phosphate) in 19 patients taking phenelzine were found to be reduced on the average to approximately 54% of the value in a control group. There was no correlation of pyridoxal phosphate level with phenelzine daily dosage over the range of 30 mg to 90 mg. No symptoms of vitamin B_6 deficiency peripheral neuropathy were found.

Key Words: phenelzine, vitamin B_6 deficiency, plasma pyridoxal phosphate

INTRODUCTION

Phenelzine, a monoamine oxidase inhibitor antidepressant, belongs to the hydrazide class of drugs, as do isoniazid and hydralazine. Both of these latter drugs are known to induce vitamin B_6 (pyridoxine) deficiency and resultant paresthesias and peripheral neuropathy. The pyridoxine deficiency and neurological signs respond to administration of vitamin B_6 (Raskin and Fishman 1965). More recently there has been one case report (Heller and Friedman 1983) and a case series of six patients (Stewart et al 1984) who were treated with phenelzine and who developed pyridoxine deficiency. In the case report, the pyridoxine deficiency was accompanied by signs and symptoms of neuropathy as well as confirmation by electromyography. However, this case was complicated by the presence of renal cell carcinoma and there was no response to pyridoxine supplementation. In the case series, symptoms suggestive of neuropathy were reported but no signs elicited. Symptoms resolved with pyridoxine supplementation. In an open prospective study of 16 subjects, Lydiard et al (1989) failed to confirm a reduction in pyridoxine levels following treatment with phenelzine although they did find low pre-treatment levels in nine patients. He suggested there was reason to suspect that patients may have been taking vitamin supplements.

This study was undertaken to determine the plasma concentration of pyridoxal phosphate (PLP) in psychiatric patients taking phenelzine compared to a control group. A newly developed high-performance liquid chromatography assay method for the measurement of serum levels of PLP was used (Yu 1989).

MATERIAL AND METHODS

Subjects were obtained through requests for referrals from the practices of all psychiatrists in Saskatoon. Inclusion criteria were that subjects be (1) between the ages of 15 and 70 years, (2) of either sex and (3) on any dosage of phenelzine for at least one week. Exclusion criteria were (1) significant physical illness, (2) ingestion of vitamin supplements in the

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Table 1

Pyridoxal phosphate serum levels (nanomolar) in patients and controls

Patients	Controls
10	112
43	20
4	41
11	37
4	13
1	77
1	99
8	54
55	96
40	57
60	68
36	60
30	101
40	64
33	50
*327 (excluded)	
31	
44	
160	
39	
median 33, mean 34.2; quartiles 8, 43;	median 60, mean 63.3; quartiles 41, 96

previous week and (3) ingestion of any drugs known or suspected to induce vitamin B_6 deficiency such as isoniazid, hydralazine, cycloserine or penicillamine. All 20 patients who were referred met the criteria for the study and all gave informed consent. On the morning of the blood test, patients and controls were instructed to take a special breakfast calculated to provide less than 0.2 mg vitamin B_6. One blood sample was drawn two to three hours after the morning dose of phenelzine.

The patients (nine male, 11 female) had a mean age of 38 years (23 to 60) and the controls (eight male, seven female) had a mean age of 35 years (20 to 52). Patients had diagnoses of panic disorder or major depression by DSM-III-R criteria (American Psychiatric Association 1987). The controls were healthy volunteers from the staff of the Department of Psychiatry and the Neuropsychiatric Research Unit. Three different daily dosages of phenelzine were prescribed: 30 mg, 45 mg and 90 mg. The duration of treatment ranged from four weeks to seven years (mean 1.9 years, mode 1.1 years).

Plasma PLP was measured by an enzymatic high-performance liquid chromatography method with a detection limit of 50 picomolar (Yu 1989).

Statistical analysis was performed using the Mann-Whitney test for the comparison of groups and the Spearman Rank correlation coefficient for the association between dose of phenelzine and plasma PLP level.

RESULTS

Table 1 shows the individual plasma PLP values for the 20 patients and 15 controls. PLP levels in patients ranged from 1 nM to 160 nM with a mean level of 34.2 nM (SE 8.2) excluding one outlier with a level of 327 nM. Controls encompassed a narrower range of 20 nM to 112 nM with a mean of 63.3 nM (SE 7.6). When the outlier was excluded, the plasma PLP levels of the patient and control groups were significantly different (Mann-Whitney Test $p = 0.002$). Including the outlier, the difference between groups was still statistically significant with $p = 0.007$. There was no correlation of PLP level with daily dose or with length of time on phenelzine. No patients reported symptoms of peripheral neuropathy.

DISCUSSION

The results of this study showed that the plasma PLP level was reduced in a group of 19 patients taking phenelzine to 54% of the level in a control group. In some individual patients the level was reduced to less than five percent of the control level. Phenelzine reacts with pyridoxal phosphate nonenzymatically to form a pyridoxalhydrazone complex and the plasma levels of PLP are assumed to be affected within hours of the ingestion of phenelzine (Bain and Williams 1960; Ebadi et al 1982; Bhagavan and Brin 1983). By binding to PLP phenelzine could potentially affect many PLP-dependent enzymes and reactions including the synthesis and catabolism of neurotransmitters, in addition to the action of phenelzine as a monoamine oxidase inhibitor.

There were no symptoms reported of parathesias or muscle weakness that might have been attributable to a peripheral neuropathy in the 19 subjects who were taking 30 mg/d to 90 mg/d of phenelzine over a period of four weeks to seven years (mean 1.9 years, mode 1.1 years). However, on the basis of these results it is not possible to state whether or not peripheral nerve changes might occur with sufficiently high doses taken for a sufficiently long period of time.

The mean level of PLP in controls of 63.3 nM in this study compares with the value of 68.6 nM in ten healthy, dietary uncontrolled volunteers measured weekly over a period of five weeks reported previously by Yu (Yu 1989) supporting the reliability of the method.

The question of whether or not patients should routinely be advised to take a vitamin B_6 supplement if they are on phenelzine was not answered by this study. However, the present results suggest that it would probably be advisable to supplement the diet with vitamin B_6 if a patient were known to be in a poor nutritional state or if there were increased demands, for example post surgery or serious physical illness.

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